

Mutations

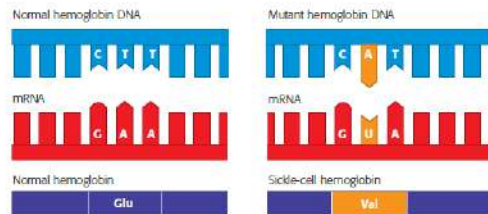
Since discovering how genes are translated into proteins, scientists have been able to describe many heritable differences in molecular terms. For instance, sickle-cell disease can be traced to a change in a single amino acid in one of the polypeptides in the hemoglobin protein (see Figure 3.19). This difference is caused by a single nucleotide difference in the DNA coding for that polypeptide (Figure 10.20).

Any change in the nucleotide sequence of a cell's DNA is called a **mutation**. Mutations can involve large regions of a chromosome or just a single nucleotide pair, as in sickle-cell disease. Occasionally, a base substitution leads to an improved protein or one with new capabilities that enhance the success of the mutant organism and its descendants. Much more often, though, mutations are harmful. Think of a mutation as a typo in a recipe; occasionally, such a typo might lead to an improved recipe, but much more often it will be neutral, mildly bad, or disastrous. Let's consider how mutations involving only one or a few nucleotide pairs can affect gene translation.

Types of Mutations

Mutations within a gene can be divided into two general categories: nucleotide substitutions and nucleotide insertions or deletions (Figure 10.21). A substitution is the replacement of one nucleotide and its base-pairing partner with another nucleotide pair. For example, in the second row in Figure 10.21, A replaces G in the fourth codon of the mRNA. What effect can a substitution have? Because

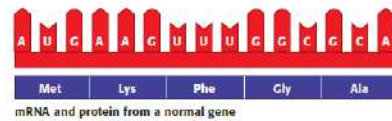
Figure 10.20 The molecular basis of sickle-cell disease. The sickle-cell allele differs from its normal counterpart, a gene for hemoglobin, by only one nucleotide (orange). This difference changes the mRNA codon from one that codes for the amino acid glutamic acid (Glu) to one that codes for valine (Val).



A single molecular "typo" in DNA can result in a life-threatening disease.

the genetic code is redundant, some substitution mutations have no effect at all. For example, if a mutation causes an mRNA codon to change from GAA to GAG, no change in the protein product would result because GAA and GAG both code for the same amino acid (Glu). Such a change is called a silent mutation. In our recipe example, changing "1¼ cup sugar" to "1¼ cup sugar"

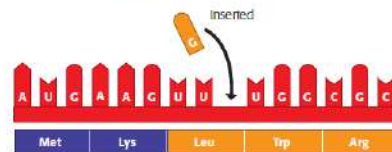
Figure 10.21 Three types of mutations and their effects. Mutations are changes in DNA, but they are shown here in mRNA and the polypeptide product.



(a) **Base substitution.** Here, an A replaces a G in the fourth codon of the mRNA. The result in the polypeptide is a serine (Ser) instead of a glycine (Gly). This amino acid substitution may or may not affect the protein's function.



(b) **Nucleotide deletion.** When a nucleotide is deleted, all the codons from that point on are misread. The resulting polypeptide is likely to be completely nonfunctional.



(c) **Nucleotide insertion.** As with a deletion, inserting one nucleotide disrupts all codons that follow, most likely producing a nonfunctional polypeptide.

would probably be translated the same way, just like the translation of a silent mutation does not change the meaning of the message.

Other substitutions involving a single nucleotide do change the amino acid coding. Such mutations are called missense mutations. For example, if a mutation causes an mRNA codon to change from GGC to AGC, the resulting protein will have a serine (Ser) instead of a glycine (Gly) at this position. Some missense mutations have little or no effect on the shape or function of the resulting protein; imagine changing a recipe from "1¼ cups sugar" to "1½ cups sugar"—this will probably have a negligible effect on your final product. However, other substitutions, as we saw in the sickle-cell case, cause changes in the protein that prevent it from performing normally. This would be like changing "1¼ cups sugar" to "6¼ cups sugar"—this one change is enough to ruin the recipe.

Some substitutions, called nonsense mutations, change an amino acid codon into a stop codon. For example, if an AGA (Arg) codon is mutated to a UGA (stop) codon, the result will be a prematurely terminated protein, which probably will not function properly. In our recipe analogy, this would be like stopping food preparation before the end of the recipe, which is almost certainly going to ruin the dish.

Mutations involving the deletion or insertion of one or more nucleotides in a gene, called frameshift mutations, often have disastrous effects (see Figure 10.21b and c). Because mRNA is read as a series of nucleotide triplets during translation, adding or subtracting nucleotides may alter the triplet grouping of the genetic message. All the nucleotides after the insertion or deletion will be regrouped into different codons. Consider this recipe example: Add one cup egg nog. Deleting the second letter produces an entirely nonsensical message—ado nec upe ggn og—which will not produce a useful product. Similarly, a frameshift mutation most often produces a nonfunctioning polypeptide.

Mutagens

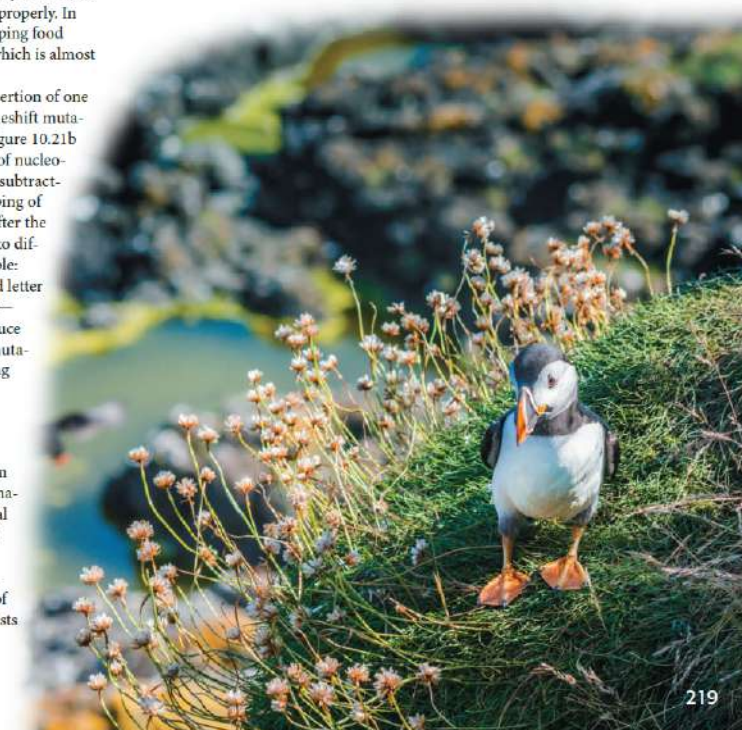
Mutations can occur in a number of ways. Spontaneous mutations result from random errors during DNA replication or recombination. Other sources of mutation are physical and chemical agents called **mutagens**. The most common physical mutagen is high-energy radiation, such as X-rays and ultraviolet (UV) light. Chemical mutagens are of various types. One type, for example, consists

of chemicals that are similar to normal DNA bases but that base-pair incorrectly when incorporated into DNA.

Because many mutagens can act as carcinogens, agents that cause cancer, you would do well to avoid them as much as possible. What can you do to avoid exposure to mutagens? Several lifestyle practices can help, including not smoking and wearing protective clothing and sunscreen to minimize direct exposure to the sun's UV rays. But such precautions are not foolproof, and it is not possible to avoid mutagens (such as UV radiation and secondhand smoke) entirely.

Although mutations are often harmful, they can also be beneficial, both in nature and in the laboratory. Mutations are one source of the rich diversity of genes in the living world, a diversity that makes evolution by natural selection possible (Figure 10.22). Mutations are also essential tools for geneticists. Whether naturally occurring or created in the laboratory, mutations are responsible for the different alleles needed for genetic research. ■

Figure 10.22 Mutations and diversity. Mutations are one source of the diversity of life visible in this scene from the Isle of Staffa, in the North Atlantic.



CHECKPOINT

1. What would happen if a mutation changed a start codon to some other codon?
2. What happens when one nucleotide is lost from the middle of a gene?

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